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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,060	01/10/2006	Naoto Hagiwara	284206US0PCT	3962

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EXAMINER	
STAPLES, MARK	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
05/20/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/564,060	HAGIWARA, NAOTO	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-14,19-34,36-43 and 48-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-14,19-34,36-43 and 48-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/04/2008 has been entered.

2. Applicant's amendment of claims 1, 9, 28-30, and 38 and the cancellation of claims 6,15-18, 35, and 44-47 in the paper filed on 01/24/2008 is acknowledged.

Claims 1-5, 7-14, 19-34, 36-43, and 48-56 are pending and at issue.

Applicant's arguments filed on 01/24/2008 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Rejections that are Withdrawn

Cancelled Claim Rejections Withdrawn

3. The rejections of cancelled claims 6, 15-18, 35, and 44-47 are moot and therefore are withdrawn.

Claim Rejections Withdrawn - 35 USC § 103(a)

4. The rejections of claims 1-5, 7-14, 19-34, 36-43, and 48-56 under 35 USC § 103(a) are withdrawn. Applicant's arguments have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Misako et al., Schelper et al., and Burns et al. (United States Patent No. 6,379,929 issued April 30, 2002).

New Rejections

Claim Rejections - 35 USC § 103

5. Claims 1, 2, 4, 5, 6, 7-9, 11-14, 19, 21, 24, 25, 27-31, 33-38, 40-43, 48-50, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al. (JP 2003-174900, published on 24.06.2003, previously cited), Schelper et al. (1997, previously cited) and Burns et al. (United States Patent No. 6,379,929 issued April 30, 2002).

Regarding claims 1, 2, 4, 5, 7, 9, 11-14, 19, 21, 24, 25, 27-31, 33-38, 40-43, 48-50, and 56 Misako et al. teach a nucleic acid amplification device comprising a first treatment chamber wherein a sample solution containing nucleic acid is heated and the

nucleic acid therein is denatured into single strands, a second treatment chamber wherein the single-stranded nucleic acid obtained in the aforementioned first treatment chamber is annealed to a primer, and a third treatment chamber wherein DNA polymerase acts upon the nucleic acid obtained in the second treatment chamber and a lengthening reaction is performed thereby. In addition, Misako et al. describe the immobilization of the DNA polymerase, a nucleic acid synthetase, in the reaction vessel and the formation of a circulatory flow route containing the aforementioned first, second, and third treatment chambers in the device (see especially Claims 11 to 13; Figure 3).

Regarding claims 4, 24, 25, and 33, Misako et al. teach that polymerase is immobilized on an inner wall surface, since the DNA polymerase is fixed in the reactor where the amplification takes place. The amplification components being fluid must be contained within the reactor (see especially Claims 11 to 13; paragraph 0023; and Figure 3).

Regarding claims 5, 12, 13, and 14, The "first treatment chamber" of Misako et al. is equivalent to the "denaturation region" of this application, and the "second treatment chamber" and "third treatment chamber" are formed in succession and are equivalent to the "regeneration region" of the instant application.

Regarding claims 21 and 50, Misako et al. teach that the number of cycles can be in the range of one to 40 (see paragraph 0068) which encompasses the range of 20 to 40 cycles of the instant claim.

Regarding claim 19; Misako et al. teach that the flow channel can comprise either the denaturation region or the regeneration region.

Misako et al. teach as noted above.

Regarding claims 1 and 9, Misako et al. teach a nucleic acid synthetase but do not specifically teach where the temperature of the regeneration region is controlled at 30 to 40°C.

Further regarding claim 30, Misako et al. teach that reagent volumes can be varied and also as referenced (see paragraph 0006) to U.S. Patent Nos. 4,683,195, 4,683,202 and 4,965,188. The device of Misako et al. is capable of performing the intended use of varying volume, thus it meets the claim limitation. Further regarding claims 27 and 56, Misako et al. teach a device of various dimensions capable of performing the intended use of the device of the instant claims. The specific dimensions recited in instant claim 56 are not critical to the claimed invention.

Regarding claims 1, 9, and 35 and further regarding claims 28, 29, and 44-47, Schelper et al. teach: "The temperature optimum of C. symbiosum polymerase [a type of nucleic acid synthetase] in our activity assay was found to be between 38°C and 42°C" (see 4th sentence of 1st full paragraph on p. 7810) which overlaps the 30 to 40°C range of the instant claims.

Regarding claims 1, 9, and 35 and further regarding claims 28, 29, and 44-47, Schelper et al. teach that C. symbiosum polymerase which is a type of nucleic acid synthetase is heat labile and had a halfilife of 10 minutes at 46°C (see Abstract).

Regarding claims 1 and 9, Schelper et al. do not specifically teach where the temperature of the regeneration region is controlled at 30 to 40°C.

Regarding claims 1 and 9, Burns et al. teach temperature controlled regions/chambers (see column 4 lines 5-21) in devices, chips, wafers, or an analytical apparatus or system and specifically teach temperature control at 30°C to 40°C (and temperatures above and below this, see column 14 lines 44-56) for use with a polymerase, replicase, or other amplification system (see column 14 lins 33-35) including mesophilic enzymes that are generally thermal labile above 37 to 42°C (see column 14 line 24).

Further regarding claim 1 and 9, Burns et al. teaches that denaturation can be done in the device with heat prior to amplification (see column 19 lines 56-62). Burns et al. also teach annealing/regenerating a primer to the nucleic acid template after heat denaturation (see column 51 lines 48 and 49). Burns et al. discloses this and other techniques (see column 3 lines 44-57 and column 48 lines 19-23).

Regarding claim 8, Burns et al. teach: “In one embodiment for mixing, after the conveying of step, the flow direction is reversed” (see column 36 lines 3-7).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al. by having a temperature control region at 30°C to 40°C with a polymerase or synthetase as suggested by Schelper et al. and Burns et al. with a reasonable expectation of success. The motivation to do so is provided by Schelper et al. and Burns et al. who teach nucleic acid amplification can be accomplished by a polymerase with a temperature in the range of 38 to 40°C and should be in that temperature range for mesophilic enzymes. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

6. Claims 3, 10, 13, 20, 22, 23, 32, 39, 51-54, are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al., Schelper et al., and Burns et al. as applied to claims 1, 2, 21, and 30 above, and further in view of Moses et al. (1994 previously cited).

Misako et al., Schelper et al., and Burns et al. teach as noted above.

Regarding claims 3 and 10, Misako et al. teach immobilizing a polymerase but do not specifically teach a immobilizing a polymerase or other nucleic acid synthetase on beads.

Regarding claim 13 and as noted above, Misako et al. teach that the flow channel can comprise either the denaturation region or the regeneration region.

Regarding claim 20 and as noted above, Misako et al. teach that the flow channel can comprise the denaturation region and the regeneration region.

Regarding claim 25 and as noted above, Misako et al. teach that the synthetase is immobilized on the inner wall of the regeneration region.

Regarding claims 3, 10, 22, 32, and 51, Moses et al. teach DNA polymerase, a type of synthetase, bound to beads which fill a column (entire reference, especially Figure 2).

Regarding claims 23, 52-54, Moses et al. teach two types/forms of DNA polymerase, a type of synthetase (see Abstract).

Further regarding claim 53 and 54, as Misako et al. teach synthetases can be immobilized on a surface/inner wall and Moses et al. teach that two types of synthetases can be immobilized on beads which is a type of surface, it was obvious from the teaching of Misako et al. in view of Moses et al. that two synthetases could be immobilized on a surface/inner wall.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al., Schelper et al., and Burns et al. by immobilizing a nucleic acid synthetase on beads as suggested by Moses et al. with a reasonable expectation of success. The motivation to do so is provided by Moses et al. who teach that the polymerase can be bound to beads, retain activity and that reagents can be passed over the beads. Further motivation is provided by Misako et al. who teach that immobilized polymerase can be used to amplify DNA. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

7. Claims 5 and 12-14 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al., Schelper et al., and Burns et al. as applied to claims 1, 2, and 4 above, and further in view of Hideo et al. (JP 6-30776 A, published on 08.02.1994, previously cited).

Misako et al., Schelper et al., and Burns et al. teach as noted above.

Misako et al. teach denaturation and regeneration regions but do not teach where they alternate each other in the flow channel.

Burns et al. teach that there can be four alternate regions of temperature control in a loop (see column 35 lines 30-39).

Regarding claims 5 and 12-14, Hideo et al. teach where denaturation and regeneration regions alternate each other in the flow channel (especially Figures 1 and 2 and where in Figure 2 the coil involves more than one loop and thus inherently alternates the denaturation and regeneration regions. It is further noted that Figure 2 of Hideo et al. is the same construction as Figure 5 of the instant application and they achieve the same thing, alternating regions of denaturation and regeneration).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the device of Misako et al., Schelper et al., and Burns et al. by alternating regions of denaturation and regeneration as suggested by Hideo et al. with a reasonable expectation of success. The motivation to do so is provided by Hideo et al. who teach that coils can be used to have flow going through alternating regions of denaturation and regeneration. Motivation to do so is also provided by Burns et al. who teach alternating regions of temperature control in a

loop. Thus, the claimed invention as a whole was prima facie obvious over the combined teachings of the prior art.

8. Claims 26 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Misako et al., Schelper et al., and Burns et al. as applied to claims 1 and 30 above, and further in view of Belfort (1988).

Misako et al., Schelper et al., and Burns et al. teach as noted above.

Misako et al., Schelper et al., and Burns et al. do not teach a flow channel comprising a semi-permeable capillary.

Regarding claims 26 and 55, Belfort teaches flow channels with semi-permeable/ permselective membrane capillaries (entire article, especially Figure 5, its description in the 1st paragraph on p. 1051 and the teaching at the bottom of p. 1052 continued to p. 1053: "In the standard design, many hollow fiber membranes are potted together at each end and sealed in a housing (usually tubular in design) so as to separate the extracapillary space (ECS) from the lumen space . . . ").

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the flow channel of Misako et al., Schelper et al., and Burns et al. by using semi-permeable/permselective membrane capillaries as suggested by Belfort with a reasonable expectation of success. The motivation to do so is provided by Belfort who teaches: " . . . reactions are conducted in solution by the whole cells or enzymes and the membranes act solely as selective

barriers"(see 1st sentence on p. 1061). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

9. No claim is free of the prior art.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples

/M. S./
Examiner, Art Unit 1637
May 12, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637